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Work during the first year of funding resulted in development of a high resolution echo planar imaging sequence for our whole-body GE SIGNA scanners. This sequence was tested in phantoms and volunteers. During the second year of funding, we increased the number of normal volunteers scanned (n=15) and scanned women with biopsy-confirmed breast cancer (n=7) and women with suspicious lesions on mammography (n=5). We developed and implemented improved methods of data analysis and performed quantitative comparisons of high spectral and spatial resolution (HiSS) images with conventional images. These comparisons demonstrate that under our experimental conditions HiSS provides improved fat-suppression, improved contrast, texture, edge delineation, and increased sensitivity to contrast media, relative to conventional MRI. These results are described papers in press in Radiology and Academic Radiology as well as another manuscript in progress.

At the same time, we have continued to develop software for our GE scanners and now have a version of high resolution EPSI that runs on our recently upgraded SIGNA scanners. This version of the pulse sequence is incorporated into the standard clinical breast imaging protocol this will allow us to increase the number of patients who are scanned after informed consent is obtained.

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(2) **INTRODUCTION:** Narrative that briefly (one paragraph) describes the subject, purpose, and scope of the research.

The goal of this research is to use high spectral and spatial resolution (HiSS) MR imaging to improve images of human breast. Our work on the application of HiSS to improve anatomic and functional imaging was first described in a paper in Academic Radiology [1]. Related work from this laboratory is presented in a number of other publications [2-9]. Work from other laboratories shows that closely related methods also provide advantages for anatomic [10] and functional [11-14] MRI.

This significant body of work provides support for the feasibility of ongoing experiments in this laboratory. Specifically, we expect to 1) improve separation of water and fat signals 2) increase image contrast 3) increase sensitivity to contrast agents and to local physiology – and as a result improve detection of suspicious lesions such as cancers and particularly delineation of tumor edges. We expect that this will increase the sensitivity and specificity of MR scans for breast cancer. To achieve these goals our original 'statement of work' was as follows:

A. Implementation of FSI methods on a clinical Scanner: Our clinical whole body scanners will be programmed to produce oscillating gradients during the decay of the proton FID so that a series of gradient echoes can be detected following excitation.

B. Processing FSI Data: Spectral information in FSI data sets will be analyzed to reduce the effects of resonance offset in MR images. Then the corrected FSI data will be used to synthesize images in which intensity is proportional to the peak intensity, linewidth, integral, and resonance frequency of resonances.

C. A phantom which contains large magnetic susceptibility gradients and both lipid and water compartments will be constructed to allow evaluation and optimization of FSI methods. Conventional spectroscopic images which use only phase encoding gradients to obtain spatial information will provide 'gold standard' images of the phantom.

D. Studies of patients: Women who are at increased risk for breast ca ncer and attend our 'high risk' clinic, and patients who are treated with neoadjuvant therapy for breast cancer will be recruited for MR studies:

1. Approximately 25 patients per year will be studied using fast spectroscopic imaging without contrast agents. **FSI** will be correlated quantitatively with conventional MRI and biopsy.

2. Approximately 25 patients per year will be given contrast. Time resolved FSI images of contrast uptake will be analyzed to measure rates of contrast uptake and accurately identify the boundaries of enhancing regions. T_1-weighted and T_2*-weighted images of contrast agent uptake will be synthesized. **FSI** images will be correlated quantitatively with conventional MRI and biopsy

3. Quantitive analysis of FSI data and quantitative comparison with conventional images: We will extend previous work of Drs. Guilhuijs and Giger to provide quantitative analysis of **FSI** and conventional images. We will compare edge sharpness, texture, temporal and spatial gradients in contrast media uptake, signal-to-noise ratio, and contrast-to-noise ratio in FSI and conventional MR images.

E. MR data will be correlated with biopsy, conventional MR images, and mammography.

(3) **BODY:**

During the 2nd budget year we made significant progress towards achieving the specific aims of the proposal. We have worked towards completion of all of the components of the statement of work listed above:

SOWA: Upgraded our FSI pulse sequence so that we can perform fast echo planar spectroscopic imaging on the new GE scanners that were recently installed at the University of Chicago. The new sequence (referred to as the following as high resolution spectroscopic imaging – or HiSS) is integrated into the standard clinical breast exam so that it is more efficient to study a larger number of patients.

SOWB. We continued development of methods for processing the data and quantitative comparison of HiSS datasets with conventional MRI.

At the same time – we continued limited studies of rodents to help us to optimize data collection and processing. In particular, we have acquired high spectral and spatial resolution images of rat brain – because the well defined anatomy allows us to evaluate the data acquisition and processing. As before, the costs of the rat experiments are not supported by this grant, but the work contributes to our implementation of HiSS.

SOWD. We have increased the number of patients and volunteers studies. Specifically we imaged normal volunteers (n=15) and women with biopsy-confirmed breast cancer (n=7) and women with suspicious lesions on mammography (n=5). We demonstrated quantitatively that fat-suppression, edge delineation, and image texture were improved in images derived from HiSS data compared to conventional images. HiSS data acquired pre- and post- contrast media injection showed features not evident in conventional images.

The work is described in detail in the manuscripts that are included.

(4) **KEY RESEARCH ACCOMPLISHMENTS:** Bulleted list of **key** research accomplishments emanating from this research

- Upgrades of fast HiSS MR imaging methods on new clinical scanners. The HiSS pulse sequences can not be integrated into standard clinical scans
- HiSS scans of breast of healthy volunteers, women with suspicious breast lesions, and women who are being treated for breast cancer.
- Quantitative analysis of HiSS and conventional image texture and edge delineation – demonstrating that HiSS increases these measures of image quality.

(5) **REPORTABLE OUTCOMES:**:

– manuscripts, abstracts, presentations;

- A paper describing aspects of this work has been accepted for publication in Radiology. We attach the manuscript. This is an important step forward for this work since it will describe this technology to Radiology's very large audience of practicing academic Radiologists and hopefully encourage them to evaluate it in their own institutions.
- An invited paper in Academic Radiology (in press) further demonstrates advantages of HiSS MRI of breast compared to conventional MRI.
- We are in the process of writing a second paper that analyzes the requirement for high spectral resolution, and compares high spectral and spatial resolution images to those obtained using the Dixon method – which uses only two points of spectral resolution.
- A third paper which reports related research on the inhomogeneous broadening of water resonances in tumors in press in NMR in Biomedicine.
- We presented the work at last year's ISMRM and are submitting two abstracts to this year's ISMRM (International Society of Magnetic Resonance in Medicine). I was also invited to present the work at the Contrast Media Research Association meeting this summer.

List of papers in press or in preparation:

1. Karczmar GS, Du W, Bick U, MacEneany P, Du Y, Fan X, Zamora M, Lipton M; Spectrally inhomogeneous effects of contrast agents in breast lesions detected by high spectral and spatial resolution MRI; Academic Radiology, in press

2. Du W, Du Y, Bick U, Fan X, MacEneany P, Zamora M, Medved M, Karczmar GS; High spectral and spatial resolution MR imaging of breast – preliminary experience. Radiology, in press.

3. Medved M, Du W, Du Y, Bick U, Fan X, MacEneany P, Zamora M, Karczmar G; Effect of increased spectral resolution on water-fat separation in breast MR imaging. Manuscript in preparation for Journal of Magnetic Resonance Imaging

– degrees obtained that are supported by this award;

Al-Hallaq- Ph.D . awarded July, 2000

Weiliang Du, PhD. Expected 2002

– funding applied for based on work supported by this award;

1. We have applied for a DOD 'Clinical Bridge Award' to continue and expand the work supported by the present grant.

2. We sent a proposal to the Army's prostate cancer research program to extend the present work to improve imaging of the prostate. This proposal was recently recommended for funding by the Army DAMD17-02-1-0033.

3. We submitted a proposal to NIH to further develop high spectral and spatial resolution MRI based on studies of rodent tumor models. This proposal received a good priority score (160) and it appears likely that funding will be awarded.

4. This work was a critical component of an instrumentation proposal to NIH that requested funding for a whole body scanner. The scanner would greatly enhance our

clinical research capability and allow us to scan a much larger number of women with breast lesions and greatly reduced cost.

CONCLUSIONS: Our results to date demonstrate quantitatively that there are significant advantages associated with high spectral and spatial resolution imaging. These include

1. Greatly improved suppression of fat signals in breast
2. Improved delineation of edges, for example tumor boundaries
3. Greatly increased sensitivity to contrast agents.
4. Potential for sensitivity to subvoxelar environements – perhaps microscopic environements represented by the various components of inhomogeneously broadened water resonances.

During the coming year we hope to expand the number of patients and volunteers we scan and further improve our methods for data analysis. We anticipate that the no. of patients scanned by the end of the funding period will be sufficient to allow more definitive comparison of HiSS and conventional MRI and perhaps a preliminary estimate of the sensitivity and specificity of HiSS MRI for malignancies.

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APPENDIX

1. Karczmar GS, Du W, Bick U, MacEneany P, Du Y, Fan X, Zamora M, Lipton M; Spectrally inhomogeneous effects of contrast agents in breast lesions detected by high spectral and spatial resolution MRI; Academic Radiology, in press

2. Medved M, Du W, Du Y, Bick U, Fan X, MacEneany P, Zamora M, Karczmar G; High spectral and spatial resolution MRI aids water-fat separation in MRI of the breast. Abstract submitted to the International Society of Magn. Reson. In Med, 2002 meeting.

3. Fan X, Du W, MacEneany P, Zamora M, Karczmar G; Using high spectral and spatial resolution MRI to detect inhomogeneous broadening of the water resonance in rat brain; Abstract submitted to the International Society of Magn. Reson. In Med, 2002 meeting.